REMARKS

Reconsideration of the present Application in view of the Amendment and Request for Continued Examination enclosed herewith and the following remarks is respectfully requested. An Amendment and Response were properly submitted to the PTO on February 4, 2005 in response to an Office Action dated January 12, 2005. As noted in the Advisory Action mailed by the PTO on February 23, 2005, the Remarks were considered; however, the Amendments were not entered.

Claims 58-71 are pending. Claims 58-63, 65, and 71 have been amended to correct a typographical error and to define more clearly certain embodiments of the invention. Support for these amendments is provided throughout the specification and does not, therefore, constitute new matter. Support for the amended claims may be found throughout the specification, for example, at page 10, lines 6-12; page 10, line 23 through page 11, line 1; page 11, line 22 through page 12, line 1; page 11, lines 27-28; page 39, line 23 through page 40, line 1; and page 42, line 14 through page 43, line 4. Additional support for amended claim 71 may be found in the specification, for example, at page 26, line 22 through page 27, line 2, and at page 50, lines 11-22.

Rejection Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 58-71 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. The Action asserts that the previously submitted claims contain new subject matter that was not described in the specification. Specifically, the Action asserts that in claims 58, 59, 62, 63, and 65, the feature "establishes concurrently a discriminatory image of antigen expression" cannot be found in the specification and that the phrase "[i]mages are captured and analyzed" (specification, page 47, lines 15-23) is different than the phrase recited in the claims. In addition, the Action asserts that in claim 71, the recitation "bound to protein G that is first coated on the solid support" cannot be found in the specification. Lastly, it is asserted that the specification discloses that the array is initially coated with a "recombinant, truncated form of protein G" and that this feature is different from "protein G."

Applicants respectfully traverse this basis of rejection and submit that the present claims as amended herein are described in the instant specification in sufficient detail such that a skilled artisan would appreciate that Applicants had possession of the invention as claimed. Applicants' presently claimed embodiment of the invention is related to an assay device for determining the presence of cancer or a propensity to develop cancer. The device comprises an array of immunoglobulin molecules, or derivatives thereof, that are immobilized to discrete regions on a solid support, wherein each discrete region comprises an immunoglobulin, or derivative thereof, that is specific for a different cell surface antigen on the same cell. When the immunoglobulin molecules interact with a biological sample comprising a cell that expresses the respective cell surface antigen, interactions between the immunoglobulin molecules and their respective cell surface antigens provide a differential pattern of density that is indicative of the presence of cancer or a propensity to develop cancer. Applicants submit that the claimed device that detects a differential pattern of density of antigen expression is described throughout the specification, including working examples, and that no new matter has been added to the application (*see, e.g.,* specification, at page 10, line 23 through page 11, line 1; page 11, lines 27-28; page 11, line 22 through page 12, line 1; page 39, line 23 through page 40, line 1; page 42, lines 14-22; Examples).

With respect to claim 71, Applicants respectfully submit that the use of protein G for immunochemistry purposes, based on the property that protein G binds to immunoglobulins, is well known and commonly practiced by persons skilled in the immunochemistry art. Accordingly, as recited in the claims and described in the specification, a skilled artisan would readily recognize that Applicants possessed the claimed device wherein the immunoglobulins or derivatives thereof are bound to protein G that is first coated on the solid support. Nevertheless, solely to advance prosecution of this application, Applicants have amended claim 71 and respectfully submit that the grounds for rejection have been obviated. This claim is presently directed in pertinent part to an assay device as recited, wherein the immunoglobulins or derivatives thereof are bound to recombinant, truncated protein G that is first coated on the solid support (*see* specification, page 50, lines 11-15).

Accordingly, Applicants submit that the present claims are fully supported by the instant specification and do not constitute new matter, meeting the written description requirements under 35 U.S.C. § 112, first paragraph. Applicants therefore respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102(b)

Claims 58-70 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Yoshinari et al. (*Br. J. Cancer* 74:359-67 (1996)). The Action asserts that Yoshinari et al. describe an ELISA device comprising an array of four monoclonal antibodies that bind to different surface antigens present on A549 lung carcinoma cells. The Action further asserts that the features in the claims describe the intended use of the claimed device and that, therefore, the claimed device is not distinguishable from the device described in Yoshinari et al.

Applicants respectfully traverse this basis of rejection and submit that Yoshinari et al. fail to anticipate the presently claimed embodiment of the invention. Applicants' invention is directed in pertinent part to an assay device for determining the presence of cancer or a propensity to develop cancer, the device comprising an array of immunoglobulin molecules, or derivatives thereof, immobilized to discrete regions on a solid support, wherein each discrete region comprises an immunoglobulin, or derivative thereof, specific for a different cell surface antigen on the same cell, and when the immunoglobulin molecules interact with a biological sample comprising a cell expressing the respective cell surface antigen, interactions between the immunoglobulin molecules and their respective cell surface antigens, a pattern of the immobilized immunoglobulins to their respective antigens provides a differential pattern of density that is indicative of the presence of cancer or a propensity to develop cancer.

Yoshinari et al. fail to teach each and every element of the claimed assay device. The document fails to teach or suggest an assay device that comprises a solid support to which an array of immunoglobulin molecules are immobilized. Yoshinari et al. also fail to teach or suggest that the array of immunoglobulin molecules is contacted by a biological sample that comprises a cell, which expresses different cell surface antigens that interact with different

immunoglobulin molecules that comprise the array. By contrast, Yoshinari et al. describe plating and culturing different cell lines in microtiter plates and detecting binding of several antibodies having different specificities to the various different cell lines. Yoshinari et al. simply do not teach or suggest a device comprising a solid support to which an array of different immunoglobulins are immobilized, which bind to different cell surface antigens on the *same* cell. Therefore, the cited document fails to teach or suggest that the interactions between the array of immunoglobulin molecules and the cell surface antigens provide a differential pattern of density indicative of the presence of cancer.

Accordingly, Applicants respectfully submit that the claimed assay device meets the requirements for novelty under 35 U.S.C. § 102 and request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

Claims 58-71 stand rejected under 35 U.S.C. § 103(a). The Action alleges that a person having ordinary skill in the art would find the claimed subject matter obvious over Yoshinari et al. in view of Pestronk et al. (*Neurology* 49:1289-92 (1997)). The Action further alleges that Yoshinari et al. describe the limitations of claims 58-70 and that Yoshinari et al. in combination with Pestronk et al. describe the features of claim 71. The Action asserts that Pestronk et al. describe covalent linkage of GM1 to an ELISA plate to which an immunoglobulin specifically binds and that Pestronk et al. thus describe covalent binding of an immunoglobulin to an ELISA plate.

Applicants respectfully traverse this rejection and submit that Yosinari et al. alone or in combination with Pestronk et al. fail to teach or suggest the subject matter of the pending claims. Applicants respectfully submit that the PTO has not established a *prima facie* case of obviousness (*see In re Mayne*, 104 F.3d 1339, 1341-43, 41 U.S.P.Q.2d 1451 (Fed. Cir. 1997) (The PTO has the burden of showing a *prima facie* case of obviousness.)). The PTO must show (1) that the references teach or suggest all claim limitations; (2) that the references provide some teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce the claimed invention; and (3) that the combined teachings of the references indicate that by combining the references, a person having ordinary skill in the art will achieve the

claimed invention with a reasonable expectation of success. When rejection of claims depends upon a combination of prior art references, something in the prior art as a whole must suggest the desirability, thus the obviousness, of making the combination (*see In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998)).

Applicants submit that alone or in combination with Pestronk et al., Yoshinari et al. fail to teach or suggest every limitation of the pending claims. As discussed above regarding the novelty of the claimed assay device, Yoshinari et al. fail to teach or suggest an assay device that comprises a solid support to which an array of immunoglobulin molecules are immobilized. Yoshinari et al. also fail to teach or suggest that the array of immunoglobulin molecules is contacted by a biological sample that comprises a cell, which expresses different cell surface antigens that interact with different immunoglobulin molecules that comprise the array. Yoshinari et al. do not teach or suggest a device comprising a solid support to which an array of different immunoglobulins are immobilized, which bind to different cell surface antigens on the *same* cell.

Contrary to the assertion in the Advisory Action (dated February 23, 2005), the problem solved by Yoshinari et al. was not an "improvement for generating antibodies by overcoming the difficulties of immobilization on glass slides by using a cells ELISA." Yoshinari et al. sought to improve screening for human monoclonal antibodies over the "commonly done ... immunohistochemical staining using formalin-fixed and paraffin-embedded tissue sections of tumour specimens" (*see* page 359, column, 1st paragraph). Accordingly, Yoshinari et al. performed immunohistochemistry comparing formalin fixation of tissues with fixation of tissue using acetone-methyl benzoate-xylene (*see, e.g.,* abstract; page 360, 1st column, 2nd and 3rd paragraphs; page 365, 2nd column, last sentence, 1st paragraph of discussion). Indeed, Yoshinari et al. observed that the acetone-methyl benzoate-xylene fixation method for tissues was effective for screening antibodies (*see* page 365, 2nd column, last paragraph). Applicants submit that this disclosure of an immunohistochemical technique fails to motivate, suggest, or teach that a modification of the method is desirable, such that an ordinarily skilled artisan would be motivated to obtain or would reasonably expect to obtain with any success Applicants' claimed assay device.

Furthermore, the cell-based ELISA described by Yoshinari et al. employed a commonly used glutaraldehyde cell fixation method, which as noted in the method described therein, was described as early as 1982 (*see* page 360, 2nd column, last paragraph). At best, Yoshinari et al. describe an immunoassay that uses a device comprising whole cells as the antigen source for screening monoclonal antibodies, which device entirely lacks each and every element of the presently claimed invention. Accordingly, the cited document absolutely fails to teach or suggest that the interactions between an array of immunoglobulin molecules on a solid support and their respective, different cell surface antigens on a cell provide a differential pattern of density indicative of the presence of cancer. Thus, Yoshinari et al. provide no motivation, teaching, or suggestion to modify the teachings therein such that an ordinarily skilled artisan would have any expectation of success to obtain Applicants' invention, which is an entirely different assay device.

With respect to claim 71, Pestronk et al. fail to remedy the deficiencies of Yoshinari et al. Claim 71 is directed in pertinent part to the assay device, wherein the immunoglobulins or derivatives thereof are bound covalently to the solid support or wherein the immunoglobulins or derivatives thereof are bound to a recombinant, truncated protein G that is first coated on the solid support. Pestronk et al. describe an immunoassay for detecting anti-GM1 ganglioside antibodies in which serum IgM is allowed to bind to GM1 ganglioside that is covalently bound to secondary amino groups on an ELISA plate. Binding of an immunoglobulin specifically to an antigen depends upon non-covalent interactions. If the serum IgM tested in the assay described by Pestronk et al. were to be covalently bound to the ELISA plate, all serum IgM would bind, which renders the assay inoperable for its purpose. Applicants therefore submit that noncovalent binding of an immunoglobulin to an antigen that is covalently bound to an ELISA plate would *not* be understood by a person skilled in the art to include the interpretation that the immunoglobulin was covalently bound to the plate. Accordingly, Pestronk et al. provide no motivation, teaching, or suggestion to a person having ordinary skill in the art to covalently bind an array of immunoglobulins to a solid surface.

Applicants respectfully submit that the present claims satisfy the requirement for nonobviousness under 35 U.S.C. § 103 and request that this rejection be withdrawn.

Applicants respectfully submit that all claims in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. In the event that the Examiner believes a teleconference will facilitate prosecution of this case, the Examiner is invited to telephone the undersigned at 206-622-4900.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

Mae Joanne Rosok
Registration No. 48,903

701 Fifth Avenue, Suite 6300
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

579390_2.DOC